Reviewer’s report

Title: Relationship between Azathioprine Metabolites and Therapeutic Efficacy in Chinese Patients with Neuromyelitis Optica Spectrum Disorders

Version: 0 Date: 18 Feb 2017

Reviewer: Byung-Jo Kim

Reviewer’s report:

This is very interesting and well-written study. The authors observed correlation of AZA metabolites concentration in erythrocyte and disease activity after AZA treatment to explore utility of the metabolite as a possible biomarker for monitoring AZA efficacy. In addition, they investigated polymorphism of metabolite transporter gene to find correlation with AZA metabolite concentration.

Here are my some concerns to need more clarify

It is confusing how subjects were managed during study period after treatment of AZA. Did subjects have steroid combined with AZA? The dose of steroid were controlled? Did subjects who were relapse during the study period have rescue therapy for acute management? Even the study design whether this is prospective design or retrospective design is not clearly mentioned.

Is there any case who had worse ARR after AZA? I recommend a figure that marked every relapse after the first attack of individual subjects. The figure will be a good schematic diagram to figure out efficacy of AZA.

As the authors mentioned in discussion, decreased ARR could be related to individual factors such as disease natural course or other immunologic status. Subjects who had stronger disease activity or more severe disease course before baseline of this study could have lower AZA efficacy. However, the baseline characteristics did not well present those individual clinical characteristics

Please discuss about how we can use metabolite concentration in erythrocyte to predict AZA efficacy which act to lymphocyte for immunosuppression. I understand the erythrocyte metabolite concentration is just a possible marker for enough AZA dose for immunosuppression. So I think the sentence in conclusion should be changed like following; "---, this effect is significantly correlated to the erythrocyte concentration of its metabolites ---" In addition, is the SLC28 a gene for transporter expressed in erythrocyte membrane or lymphocyte membrane? Please discuss more clearly.

Please mention about any limitations of this study. Disease activity of NMOSD is so variable by individual subjects. We frequently observe patients who relapse many times for a year after long term quiet years, so it is hard to evaluate disease activity using ARR during only 1 or 2 years. AZA efficacy is also different individually. One year period is not enough to observe AZA
efficacy. Some patients show AZA efficacy after 6 months to 18 months to have enough drug effect. Therefore the sample number as 32 subjects is not high enough to suggest valuable conclusion.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

Nothing to declare

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal